

General

Guideline Title

Effectiveness of practices to reduce blood sample hemolysis in EDs: a Laboratory Medicine Best Practices systematic review and meta-analysis.

Bibliographic Source(s)

Heyer NJ, Derzon JH, Wings L, Shaw C, Mass D, Snyder SR, Epner P, Nichols JH, Gayken JA, Ernst D, Liebow EB. Effectiveness of practices to reduce blood sample hemolysis in EDs: a laboratory medicine best practices systematic review and meta-analysis. Clin Biochem. 2012 Sep;45(13-14):1012-32. [25 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions for the ratings of overall strength of evidence and recommendation categories can be found at the end of the "Major Recommendations" field.

Conclusions and Best Practices Recommendations

Use of straight needles for venipuncture is effective in reducing hemolysis in the emergency department (ED) and is recommended by Laboratory Medicine Best Practices Initiative (LMBP) as an "evidence-based best practice." This recommendation is on the basis of six "good" and five "fair" studies conducted in the ED that examined the effectiveness of using straight needles and consistently found "substantial" reductions in the rates of hemolyzed samples from straight needle venipuncture relative to using intravenous (IV) starts as a source for blood samples.

While the use of IV starts for collecting blood samples in the ED is associated with increased hemolysis and should be avoided, it is assumed that this common practice may continue for some time. Indeed, the "Infusion Nursing Standards of Practice," published in a supplement to the January/February 2011 issue of the *Journal of Infusion Nursing*, discusses phlebotomy using vascular access devices including several warnings.

Evidence exists for practices that can improve hemolysis results when IV starts are used. Four studies, three rated "good" and one rated "fair" examined the effectiveness of drawing blood from an IV start placed at the antecubital site rather than a more distal site. Each of these studies reported "substantial" reductions in hemolysis when drawn from an antecubital site relative to a more distal site. Thus, when the decision to use an IV start for collecting blood samples in the ED has been made, then the use of antecubital sites is recommended by LMBP as an evidence-based best practice to reduce the rates of hemolyzed samples.

In addition, consistent and "substantial" reduction in hemolysis was observed in the two studies contrasting the effectiveness of low vacuum tubes in reducing hemolysis relative to regular vacuum tubes in the ED. However, with only one "good" and one "fair" study providing evidence for the effectiveness for this practice, the overall strength of evidence for this practice is only "suggestive". Given tubes of the same size, a partial vacuum tube collects less blood than a full vacuum tube and this has been reported as an advantage when multiple draws are necessary, especially with pediatric patients.

Two practices, use of ≤ 21 gauge syringes (compared with >21 gauge syringes) and use of a syringe (rather than a vacuum tube) when collecting blood from an IV start, had "insufficient" overall strength of evidence of effectiveness for reducing hemolyzed samples in the ED.

Definitions

Overall Strength of Evidence Ratings

The revised definitions for these categories, modeled after the US Preventive Services Task Force (2008) are as follows:

High: An adequate volume of evidence is available and includes consistent evidence of substantial healthcare quality changes from studies without major limitations.

Moderate: Some evidence is available and includes consistent evidence of substantial healthcare quality changes from without major limitations.

Suggestive: Limited evidence is available and includes consistent evidence of moderate healthcare quality changes from a small number of studies without major limitations; OR the quality of some of the studies' design and/or conduct is limited.

Insufficient: Any estimate of an effect is very uncertain. Available evidence of effectiveness is:

- Inconsistent or weak; OR
- Consistent but with a minimal effect; OR
- Contained in an inadequate volume to determine effectiveness

Recommendation Categories

The recommendation rating categories are consistent with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) group findings (2008) and reflect the extent to which the available evidence gives one confidence that a practice will do more good than harm.

Recommend: The practice should be identified as a best practice for implementation in appropriate care settings, taking into account variations in implementation and/or care settings. This recommendation results from consistent and high or moderate overall evidence of effectiveness strength rating of desirable impacts.

No recommendation for or against: The potentially favorable impact on care outcomes and/or error reduction is not sufficient, or not sufficiently supported by evidence to indicate that it should be identified as a best practice for implementation in appropriate care settings. Additional studies may be warranted to strengthen the relevant evidence base. This recommendation results from insufficient evidence to determine effectiveness.

Recommend against: The practice should not be identified as a best practice for implementation because of consistent evidence of adverse effects.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Any emergency condition that requires blood sampling

Guideline Category

Diagnosis

Technology Assessment

Clinical Specialty

Emergency Medicine

Pathology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Clinical Laboratory Personnel

Hospitals

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To complete a systematic review of emergency department (ED) practices for reducing hemolysis in blood samples sent to the clinical laboratory for testing

Target Population

Patients receiving treatment in hospital-based emergency departments (EDs)

Interventions and Practices Considered

1. Straight needle venipuncture vs. intravenous (IV) start
2. Antecubital site vs. distal sites
3. Use of syringe vs. vacuum tubes
4. Use of ≤ 21 -gauge (larger) needles
5. Use of low (partial) vacuum tubes

Major Outcomes Considered

Hemolysis rates

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

The question addressed by this evidence review is: "When drawing blood samples for laboratory testing from patients in the emergency department (ED), what practices are effective in reducing hemolysis rates among these samples?" The relevant PICO elements are:

- Population: Patients receiving treatment in hospital-based EDs
- Interventions: Blood collection practices in the ED hypothesized to be associated with hemolysis rates
- Comparison: Comparison practices are generally ongoing ED practices, which include various combinations of all the practices being studied
- Outcome: Hemolysis rates are the outcomes of interest. There are two widely used methods of measuring hemolysis in centrifuged blood samples: direct spectrophotometric readings by instrument (quantitative and objective), and visual comparison of blood samples with a color chart by laboratory personnel (semi-quantitative and subjective). Hemolysis in a blood sample is a continuum, and the level of hemolysis considered significant can vary among institutions. The level at which hemolysis impacts clinical laboratory results varies by the type of test being conducted.

A comprehensive electronic search for literature was conducted with the guidance of a professional librarian from July through October 2011. It included English-language publications (or availability of an English abstract) since 1990.

Search of databases for published, peer reviewed literature as well as gray literature included the National Institutes of Health (NIH) maintained PubMed, two professional electronic databases, CINAHL (Cumulative Index to Nursing and Allied Health Literature) and EMBASE (focusing on international biomedical literature) and VHINL (Virginia Henderson International Nursing Library). The search terms used are included in Appendix C in the original guideline document. In addition, hand searches of references in identified publications were also conducted. Finally, a general request for unpublished data that may have been collected by hospital EDs for their own internal surveys was spread through contacts supplied by the Laboratory Medicine Best Practices Initiative (LMBP) Hemolysis Expert Panel.

Published studies and unpublished data were screened by at least two independent reviewers to reduce subjectivity and the potential for bias, and all differences were resolved through consensus. Initial screening of titles and abstracts was used to exclude studies from full review if it was clear they did not satisfy the following criteria: 1) address hemolysis; 2) were relevant to the ED; and 3) were related to one of the practices of interest. During full review, studies and data were eliminated if they did not: 1) address hemolysis rates in a hospital ED; 2) evaluate one of the practices of interest for effectiveness; or 3) include sufficient data in an appropriate format to constitute a study.

Number of Source Documents

A total of 545 non-duplicate bibliographic records were identified, 541 from structured searches and 4 from hand searches. In addition, 22 hospital emergency departments (EDs) responded to requests for unpublished data. The source that generated the most submissions of unpublished data for this review was a request disseminated in the newsletter of the Center for Phlebotomy Education, Inc.

The review of all 545 published titles and abstracts (see Fig. 2 in the original guideline document) eliminated 514 references as off-topic. The remaining 31 published studies were subjected to full text review. Of these, a further 17 studies were excluded for not meeting minimum criteria, and 2 were eliminated during abstraction and quality review. The remaining 12 published studies were included in the analyses.

Among the 22 institutions that offered unpublished findings, only 4 had sufficient data on the topics of interest to be included in the analysis. The most common reason for exclusion of unpublished data was the lack of denominator data (total blood draws from which the hemolyzed samples were observed). Thus, a total of 16 studies (12 published and 4 unpublished) contributed data to the review of practices to reduce hemolysis in the ED.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Strength of Evidence Ratings

The revised definitions for these categories, modeled after the US Preventive Services Task Force (2008) are as follows:

High: An adequate volume of evidence is available and includes consistent evidence of substantial healthcare quality changes from studies without major limitations.

Moderate: Some evidence is available and includes consistent evidence of substantial healthcare quality changes from without major limitations.

Suggestive: Limited evidence is available and includes consistent evidence of moderate healthcare quality changes from a small number of studies without major limitations; OR the quality of some of the studies' design and/or conduct is limited.

Insufficient: Any estimate of an effect is very uncertain. Available evidence of effectiveness is:

- Inconsistent or weak; OR
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- Contained in an inadequate volume to determine effectiveness

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Studies and data that passed full review were abstracted and evaluated for quality and evidence of effectiveness according to Laboratory Medicine Best Practices Initiative (LMBP) methods (see the "Availability of Companion Documents" field).

All abstracted results that received a "good" or "fair" study quality rating had their results converted to risk ratios, which were plotted on common graph for each practice reviewed. A grand mean estimate of the result of the practice was calculated using inverse variance weights and mixed-effects models, a valuable tool for estimating precision and assessing the consistency and patterns of results across studies. The key criteria for including studies in the meta-analyses were sufficient data to calculate an effect size and use of an outcome that is judged similar enough to the other studies being summarized.

The grand mean estimate and its confidence interval were considered more accurate representations of the results of a practice than that obtained from individual studies. By convention, all meta-analysis results are presented in tabular forest plots and are generated using Comprehensive Meta-analysis software (v. 2.2.064, Statistical Solutions). For this review, an expert review panel determined that a "substantial" effect is a reduction of hemolysis by 50%, as represented by a risk ratio of 0.5 or less.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

This evidence review followed the Center for Disease Control and Prevention (CDC)-sponsored Laboratory Medicine Best Practices Initiative (LMBP)'s "A-6 Cycle" systematic review methods for evaluating quality improvement practices (see the "Availability of Companion Documents" field). This approach is derived from previously validated methods, and is designed to produce transparent systematic review of practice effectiveness to support evidence-based best practice recommendations.

A review team conducts the systematic review and includes a review coordinator and staff trained to apply the LMBP methods. The team is guided by a multi-disciplinary expert panel including at least one LMBP Workgroup member and individuals selected for their diverse perspectives and relevant expertise in the topic area, laboratory management, and evidence review methods.

Recommendations are formulated in accordance with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group findings to reflect the extent to which one can be confident that following the recommendations will do more good than harm.

Rating Scheme for the Strength of the Recommendations

Recommendation Categories

The recommendation rating categories are consistent with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) group findings (2008) and reflect the extent to which the available evidence gives one confidence that a practice will do more good than harm.

Recommend: The practice should be identified as a best practice for implementation in appropriate care settings, taking into account variations in implementation and/or care settings. This recommendation results from consistent and high or moderate overall evidence of effectiveness strength rating of desirable impacts.

No recommendation for or against: The potentially favorable impact on care outcomes and/or error reduction is not sufficient, or not sufficiently supported by evidence to indicate that it should be identified as a best practice for implementation in appropriate care settings. Additional studies may be warranted to strengthen the relevant evidence base. This recommendation results from insufficient evidence to determine effectiveness.

Recommend against: The practice should not be identified as a best practice for implementation because of consistent evidence of adverse effects.

Cost Analysis

A cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Reduction in hemolyzed blood samples sent to the clinical laboratory for testing that can give unreliable results

Potential Harms

The recommended practice of using a straight needle for blood draws in the emergency department (ED) frequently requires an additional venipuncture. All venipuncture procedures pose a risk to ED staff of needle stick injury and exposure to infectious or other harmful agents. Venipuncture procedures should always be performed using universal precautions. Patients are also at some small risk for needle site injury when

multiple attempts are made to obtain blood samples.

Qualifying Statements

Qualifying Statements

The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).

Study Limitations

A wide variety of practices for drawing blood samples are observed in the emergency department (ED), largely determined by the personal preference of the ED medical staff person conducting the blood draw. Many of the studies summarized in this review controlled for one or two variations in those practices and allowed the others to vary without evaluation. However, their conclusions attributed all the variation in hemolysis to the practice of interest. To the extent practices are unrelated, differences in concurrent practices may increase error variation in outcome estimates. Error variance increases cross-study heterogeneity and reduces confidence in the grand mean estimated for the practice, but does not fundamentally bias the overall estimate of effectiveness for the practice. However, to the extent these practices are related, this error variance creates a bias that can systematically inflate or deflate the practice effectiveness estimate. This was considered in the evaluation of these practices.

In addition, hemolysis may not be solely the result of pre-analytic practices. As one group of authors have observed, improper centrifugation, delayed separation of specimens, and re-spinning of tubes with gel separators may each contribute to specimen hemolysis, albeit at considerably lower rates than pre-analytic collection and transport practices.

While the Laboratory Medicine Best Practices Initiative (LMBP) systematic review methods are consistent with practice standards for systematic reviews, there still remains a measure of subjectivity in evaluating studies. Bias may be subtly introduced even when consensus is used to establish relevant outcome measures and effect size rating categories (e.g., "substantial," "moderate," "minimal/none"). Other factors, such as the experience and academic disciplines of the raters, and the criteria for study inclusion/exclusion may also influence findings. The restriction to English language studies (at least for an abstract) to satisfy the requirement of multiple reviewers for each study may also introduce bias. Most of the evidence for this review is from quality improvement studies, thus the primary data are limited to a single institution and site-specific differences may impact study results and conclusions. Despite this variation among institutions, the recommended practices had consistently favorable results.

Implementation of the Guideline

Description of Implementation Strategy

Feasibility of Implementation

Straight needle venipuncture is a common practice and requires no additional training of personnel. When compared to using intravenous (IV) starts for collecting blood samples, there is a modest additional cost and time in placing both an IV and collecting blood from straight needle venipuncture, but this cost is likely mitigated when laboratory staff time to evaluate a hemolyzed sample is added to the burden of soliciting, executing, and evaluating a second draw is taken into consideration.

The antecubital fossa provides a large vein for drawing blood samples, typically with easy access, allows the use of larger needles, and is less likely to collapse. IV placement is often a matter of personal preference and training, and when tolerated by the patient's condition, no barriers to implementation are anticipated.

Implementing use of partial vacuum tubes represents a decision by the laboratory department and requires no change in staff behavior. Use of partial vacuum tubes is likely applicable across all other alternative practices except the use of a syringe, where it directly competes as a method of reducing the applied vacuum.

Implementation Tools

Resources

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Heyer NJ, Derzon JH, Wings L, Shaw C, Mass D, Snyder SR, Epner P, Nichols JH, Gayken JA, Ernst D, Liebow EB. Effectiveness of practices to reduce blood sample hemolysis in EDs: a laboratory medicine best practices systematic review and meta-analysis. *Clin Biochem* 2012 Sep;45(13-14):1012-32. [25 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Sep

Guideline Developer(s)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

Laboratory Medicine Best Practices - Independent Expert Panel

Source(s) of Funding

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Guideline Committee

Laboratory Medicine Best Practices Hemolysis Expert Panel

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Financial Disclosures/Conflicts of Interest

Members of the Laboratory Medicine Best Practices (LMBP™) systematic review expert panels and Workgroup are asked to provide information about financial, professional or other associations that may represent or appear to be a potential conflict related to the conduct of the LMBP™ systematic evidence reviews. The Centers for Disease Control and Prevention (CDC) LMBP™ staff reviews the conflict of interest disclosures. If a conflict arises in connection with an LMBP™ systematic review or publication, the appropriate disclosure is provided.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the [PubMed Central \(PMC\) Web site](#) .

Availability of Companion Documents

The following are available:

- Laboratory Medicine Best Practices (LMBP). Effective practices to reduce blood sample hemolysis in emergency departments. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2012 Feb. 5 p. Electronic copies: Available from the [Centers for Disease Control and Prevention \(CDC\) Web site](#) .
- Christenson RH, Snyder SR, Shaw CS, Derzon JH, Black RS, Mass D, Epner P, Favoretto AM, Liebow EB. Laboratory Medicine Best Practices: systematic evidence review and evaluation methods for quality improvement. Clin Chem 2011;57:816-25. Electronic copies: Available from the [Clinical Chemistry Web site](#) .
- Snyder S, Liebow E, Shaw C, Black R, Christenson R, Derzon J, Epner R, Favoretto A, John L, Mass D, Patta A, Rose S, Washington M. Laboratory Medicine Best Practices: developing systematic evidence review and evaluation methods for quality improvement phase 3 final technical report. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2010 May 27. 159 p. Electronic copies: Available from the [CDC Web site](#) .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on May 28, 2015. The information was verified by the guideline developer on August 13, 2015.

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